REMARKS

Reconsideration and withdrawal of the objections and rejections to the application are requested in view of the amendments and remarks made herein, which place the application into condition for allowance or into better condition for appeal.

I. STATUS OF CLAIMS AND FORMAL MATTERS

Claims 1-18 are pending in this application. Claims 1-16 are amended; claims 17 and 18 are added. Support for the amended claims is found throughout the specification. No new matter is added.

It is submitted that these claims are in full compliance with the requirements of 35 U.S.C. §112. The amendments of the claims herein are not made for the purpose of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112; but rather the amendments are made simply for clarification and to round out the scope of protection to which Applicants are entitled. Furthermore, it is explicitly stated that the herewith amendments should not give rise to any estoppel, as the herewith amendments are not narrowing amendments.

Priority

The Examiner is thanked for acknowledging Applicants' claim for foreign priority. Enclosed, in accordance with 35 U.S.C. §119(b), is a certified copy of German application 10041861.9, filed on July 6, 2000.

Claim Objections

Claims 6, 11 and 12 were objected to under 37 CFR 1.75(c) as being in improper form. Claims 4 and 6 have been amended such that they are no longer multiply dependent claims, overcoming the basis for the objections. The Examiner is thanked for examining these claims on the merits.

II. THE REJECTIONS UNDER 35 U.S.C. §101 ARE OVERCOME

Claims 1-3 were rejected under 35 U.S.C. §101 as being directed to non-statutory subject matter. The word "isolated" has been added to claims 1-3, obviating the rejection.

Claims 13 and 14 were rejected under 35 U.S.C. §101 as reciting a use without setting forth any steps involved in the process. Claims 13 and 14 have been amended, and are now proper method claims.

Reconsideration and withdrawal of the rejections under §101 are requested.

III. THE REJECTIONS UNDER 35 U.S.C. §112, 1ST PARAGRAPH, ARE OVERCOME

Claims 1-16 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking adequate written description. The rejection is traversed.

Claim 1 has been amended such that part d) is limited to sequences that hybridize under stringent conditions with those stated under parts a) or b). The term "stringent conditions" is clearly defined in the paragraph beginning on page 15, line 21 of the specification. Further, part e) has been amended to read on a sequence having at least about 75% identity with the nucleic acid sequences stated under part a).

The Office Action states on page 5 that "it is not sufficient to define DNA solely by its principal biological property". It is submitted that the DNA of the instant invention is defined both by structure and function. The structure is clearly given by SEQ ID NOs:1-8, and molecules which hybridize to nucleic acids of these sequences under stringent conditions share this defined structure. Further, molecules with at least about 75% identity to SEQ ID NO:1 are structurally defined. The function of such nucleic acid molecules is stated in the preamble to claim 1. Therefore, the DNA of the invention is defined by its structural and functional characteristics and meets the written description requirement of §112.

Claims 14 and 16 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking adequate written description and enablement. The rejection is traversed.

The Applicants have demonstrated that the promoter of the invention can provide tissue-specific expression, i.e. is a caryopsis-specific promoter. It can be used to express nucleic acids that are functionally linked to the promoter sequence, such as in an expression cassette or vector. The nucleic acid that is linked to the promoter can be a polypeptide-encoding sequence (e.g. a gene), and can be linked to the promoter in sense or anti-sense orientation. The nucleic acid may also encode a non-translatable RNA, such as an anti-sense RNA or a ribozyme.

As the promoter of the present invention is specifically active in the caryopsis of plants, it is clear to a person skilled in the art that it can be used for caryopsis-specific expression of ribozymes or anti-sense RNA. As a consequence, the effect of the expression of ribozyme or anti-sense RNA are also focussed on the respective tissue where the promoter is active.

It is well known in the art that ribozymes can attack and cleave specific RNAs so that, by expression of such ribozymes, the RNA level can be affected or knocked out. Preparation and design of anti-sense sequences and ribozymes are standard methods routinely used by the skilled

artisan. For example, Tada *et al.* (copy enclosed) have demonstrated the reduction of allergenic proteins in the caryopsis of rice using anti-sense RNA. Similarly, Zhang *et al.* (copy enclosed) have shown tissue-specific inhibition in barley via an anti-sense construct.

Far *et al.*, cited by the Examiner, is directed to the optimization of anti-sense RNA effects and the theoretical mechanisms behind it. This reference points out the advantages and difficulties of anti-sense technology in the context of providing computer-based tools to design effective suppression of target genes. The authors specifically address the problems with short chain anti-sense sequences of less than 25 nucleotides. The mere fact that the authors are attempting to improve upon a specific aspect of anti-sense oligonucleotide technology does not stand against the many reports in the art of successful anti-sense RNA inhibition.

According to the Court of Appeals for the Federal Circuit in the case of *In re Wands*, 8 U.S.P.Q. 2d 1400 (Fed. Cir. 1988),

> Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is undue, not experimentation. The determination of what constitutes undue experimentation in a given case requires the application of standard of reasonableness, having due regard for the nature of the invention and the state of the art. The test is not merely quantitative, since **a considerable amount of experimentation is permissible, if it is merely routine**, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed ... [Citations omitted].

Id. at 1404.

Against this background, determining whether undue experimentation is required to practice a claimed invention turns on weighing many factors summarized in *In re Wands* (*Id.*). For example, (1) the quantity of experimentation necessary; (2) the amount of direction or guidance presented; (3) the presence or absence of working examples of the invention; (4) the nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability or unpredictability of the art; and (8) the breadth of the claims.

In this case, detailed direction is present in the application regarding making and using the promoter as claimed in claim 1. The prior art is replete with examples of anti-sense RNA and ribozyme inhibition, and the relative skill of those in the art is high.

As with any promoter, the use of the promoter of the present invention in anti-sense RNA or ribozyme inhibition involves a certain amount of experimentation. However, there is no indication that more than routine experimentation is required to optimize the ribozyme or anti-sense sequence to be fused to the promoter of the invention in order to obtain suppression of the target gene in the caryopsis. For the purposes of this invention, the identity of the target gene is not essential. The promoter of the invention can be used wherever caryopsis-specific suppression is desirable, and there is no indication that the methods known in the art and described in Tada *et al.* and Zhang *et al.* are not applicable with the promoter of this invention, as they have been with many other promoters, as previously published in the literature.

In view of the amendments and arguments presented above, reconsideration and withdrawal of the rejections under 35 U.S.C. §112, first paragraph, are requested.

IV. THE REJECTIONS UNDER 35 U.S.C. §112, 2ND PARAGRAPH, ARE OVERCOME

Claims 1-16 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. Claim 1 has been amended to recite only one range or limitation, overcoming the rejection on this basis. Further, claims 13 and 14 have been amended to set forth steps involved in a process. The rejections under §112, second paragraph, are obviated, and reconsideration and withdrawal are requested.

V. THE REJECTIONS UNDER 35 U.S.C. §102 ARE OVERCOME

Claims 1-12 and 15 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Visser *et al.* Claims 1-8 and 11 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Steege *et al.* These rejections are traversed and will be addressed collectively.

Both Visser *et al.* and Steege *et al.* relate exclusively to potato, which is a dicot. To the contrary, the promoter of the instant invention is caryopsis-specific and was isolated from wheat, a monocot. Caryopses are only present in monocots, in particular, the grass family *Poaceae.* In this respect the promoters described by Visser *et al.* are not related to the caryopsis-specific promoter of the present invention.

Visser *et al.* and Steege *et al.* work with the same promoter and refer to one another in their publications. Thus, the promoter sequence indicated in Steege *et al.* and the fragment used by Visser *et al.* are identical. (Note that the accession number indicated by Steege *et al.*, Acc. No. X58453, lists Visser as an author.) As is demonstrated on the attached sequence alignment between the sequence listed under accession number X58453 and SEQ ID NO:1, there is only

45.5% identity between the two molecules, and consecutive identical nucleotides occur only in very short stretches.

Therefore, the statement on page 10 of the Office Action that plasmid pPGB-1 of Visser is the same as the vector taught in the instant application is misguided. The respective promoter sequences show a low level of sequence identity. The fact that the sequence in Visser *et al.* is described as "5' upstream region of the granule-bound starch synthase" does not provide any information regarding the similarity or difference in the function of that promoter and the one of the present invention. Accordingly, reconsideration and withdrawal of the rejections under §102 are requested.

CONCLUSION

Applicants believe that the application is in condition for allowance, and favorable reconsideration of the application and prompt issuance of a Notice of Allowance are earnestly solicited.

Respectfully submitted,

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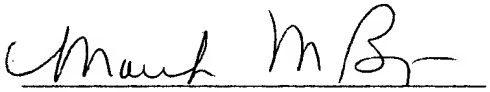
By: 

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

1. (Amended) An isolated nucleic acid molecule with the function of a caryopsis-specific promoter, which nucleic acid molecule:

f) comprises the nucleic acid sequence defined by Seq ID No. 1 or deposited by DSM 13398 (plasmid p 11/1);

g) comprises one or more sequence elements selected from the group consisting of

viii) cacgcaaagg cgcgtcggcc agccacgac (Seq ID No. 2);

ix) agaaacaaac aaacaaacaa aaaagt (Seq ID No. 3);

x) cctttcagga cgatgcttcg gtgccttaag acacctacc tttgtgtcta tgacatgtga gcccaacag atggct (Seq ID No. 4);

xi) cccgtctagg cgttcggtgt ccggcc (Seq ID No. 5);

xii) cagggagcct tcga (Seq ID No. 6);

xiii) tcagccagtt ccaccccgtg cacg (Seq ID No. 7) and

xiv) tactctggtc atgttaa (Seq ID No. 8);

h) comprises a functional portion of the nucleic acid sequence stated under a);

i) comprises a sequence which hybridizes under stringent conditions with at least one of the nucleotide sequences stated under a) and/or b); and/or

j) comprises a sequence which has approx. [60-99% identity, preferably approx.] 75-99% identity[, in particular approx. 90-99% identity and very especially preferably approx. 95-99% identity] with one of the nucleic acid sequences stated under a).

2. (Amended) [A]The isolated nucleic acid molecule as claimed in claim 1, which is a promoter that is active in plants.

3. (Amended) An expression cassette comprising [a]the isolated nucleic acid molecule as claimed in claim 1.

4. (Amended) A vector comprising [a]the isolated nucleic acid molecule as claimed in claim 1[or an expression cassette as claimed in claim 3].

5. (Amended) [A]The vector as claimed in claim 4 which is suitable for transforming plant cells.

6. (Amended) A host cell comprising[which is genetically modified with a]the isolated nucleic acid molecule as claimed in claim 1[, with an expression cassette as claimed in claim 3 or with a vector as claimed in claim 4].

7. (Amended) [A[The host cell as claimed in claim 6, which is a pro- or eukaryotic cell.

8. (Amended) [A]The host cell as claimed in claim 6, which is a plant cell.

9. (Amended) A plant comprising the plant cell[s] as claimed in claim 8.

10. (Amended) Propagation material or harvested material from the plant[s] as claimed in claim 9[, comprising plant cells as claimed in claim 8].

11. (Amended) A method of generating transgenic plant cells[as claimed in claim 8], comprising the steps of transforming[wherein] plant cells, plant tissue, plant parts or protoplasts [are transformed] with [a]the isolated nucleic acid molecule as claimed in claim 1, [a]the vector as claimed in claim 4, [with an] the expression cassette as claimed in claim 3, or [with a]the host cell as claimed in claim 6, and growing the transformed plant cells, plant tissues, plant parts or protoplasts [are grown] in a growth medium.

12. (Amended) A method of generating transgenic plants[as claimed in claim 9], comprising the steps of transforming[wherein] plant cells, plant tissue, plant parts or protoplasts [are transformed] with [a]the isolated nucleic acid molecule as claimed in claim 1, [a]the vector as claimed in claim 4, [with an]the expression cassette as claimed in claim 3, or [with a]the host cell as claimed in claim 6, growing the transformed plant cells, plant tissues, plant parts or protoplasts [are grown] in a growth medium, and regenerating intact plants [are regenerated] from these.

13. (Amended) A method[The use of a nucleic acid molecule as claimed in claim 1] for [the] caryopsis-specific expression of genes in genetically modified plants comprising transforming a plant cell, plant tissue, plant part or protoplast with the nucleic acid molecule as claimed in claim 1, wherein the nucleic acid molecule drives expression of genes under the control of the nucleic acid molecule.

14. (Amended) A method[The use of a nucleic acid molecule as claimed in claim 1] for the caryopsis-specific suppression of genes in genetically modified plants comprising

transforming a plant cell, plant tissue, plant part or protoplast with the nucleic acid molecule as claimed in claim 1, wherein the nucleic acid molecule suppresses expression of genes under the control of the nucleic acid molecule.

15. (Amended) A method for [the] caryopsis-specific gene expression in plants, wherein a nucleic acid molecule as claimed in claim 1 is stably integrated into to the genome of a plant cell, and the plant is regenerated from said plant cell.

16. (Amended) A method for [the] caryopsis-specific gene suppression in plants, wherein a nucleic acid molecule as claimed in claim 1 is stably integrated into the genome of a plant cell, and a plant is regenerated from said plant cell.